The incremental value of dual modality PET/CT imaging over PET imaging alone in advanced colorectal cancer

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Abstract

Background ^{18} Fluoro-2-Deoxy Glucose (18 FDG) positron emission tomography (PET) impacts upon the management of recurrent colorectal cancer (CRC) but is limited by anatomical localisation. The development of integrated positron emission and computerised tomography (PET/CT) yields high anatomical resolution combined with the PET data. We evaluate the added value of PET/CT over PET alone.

Method Thirty-one consecutive patients had PET/CT for suspected recurrent CRC. Two blinded observers (A and B) reported images from PET alone and from integrated PET/CT. Lesion detection, lesion localisation, diagnostic certainty and impact on surgical management was assessed for each data set and then compared. The minimum clinical follow up was for 8 months (median 9.6 months) and 7 patients had histological confirmation of diagnosis.

Results Compared to PET alone, PET/CT the percentage of lesions accurately localised increased from 96% to 99% for observer A and 86% to 99% for Observer B. PET/CT increased the number of lesions reported as definitely abnormal or normal from 78% to 95% for Observer A and from 72% to 94% for Observer B. Surgical management was changed in 6 patients (19%). Inter-observer variability was reduced with PET/CT.

Conclusion PET/CT improves the accuracy of reporting in recurrent colorectal cancer and influences surgical management in a significant proportion of patients when compared to PET only imaging.

Keywords PETCT · Advanced colorectal cancer · Surgical management

Introduction

There is growing consensus that ^{18} F-fluorodeoxyglucose positron emission tomography (FDG PET) is a successful modality in evaluating many types of cancer, including colorectal cancer. It is based on the principal that malignant cells have a high glucose-6-phosphatase activity and rapidly turnover ^{18} F-fluorodeoxyglucose, thereby increasing the signal to background ratio and creating 'hot spots'. The reported increased sensitivity of FDG PET over CT has been attributed to the ability of FDG PET to detect metabolic abnormalities that precede the morphological changes seen by CT [1].

In patients with colorectal cancer FDG PET is used for the staging of local and distant recurrent disease, including hepatic metastases [2–6]. It should be noted, that the sensitivity of FDG PET for metastatic liver lesions varies

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significantly with the size of the lesion [7]. Ruers et al demonstrated in patients with colorectal cancer metastases to the liver, that the sensitivity of FDG PET for lesions less than 1.5 cm was 14%, between 1.5 cm and 3 cm was 84% and for lesions greater than 3 cm 100% [8].

FDG PET has also been shown to be useful in the assessment of patients with a rising CEA, when other imaging modalities have failed to identify attributable cause [9–12].

With these applications of FDG PET available, FDG PET may alter patient management by improving the accuracy with which therapeutic decisions are made and there by avoiding inappropriate surgery [13–16].

There are, however, recognised limitations of FDG PET. There is the relatively poor anatomical definition. This is disadvantageous to the surgeon, especially when the planning of a precise resection is required. There is also the problem with normal physiological uptake of the tracer seen in the digestive tract and genitourinary system, which can lead to false positives and lower specificity [17–19].

In an attempt to combat these limitations technological progress has led to image fusion of high resolution computerised tomography (CT) with the functional images of PET by combining these individual imaging technologies in a single integrated machine, PET/CT scanner [20] (Fig. 1). Such a machine allows the multi-disciplinary team to acquire accurately aligned anatomic and functional images for a patient from a single scanning session.

The clinical impact of such technologies is yet to be fully assessed in patients with advanced colorectal tumours. Therefore, using patients from our cancer collaborative, we assessed the use of FDG PET/CT in these patients and compared it to the findings with PET alone.

Materials and methods

Patients

Thirty-one consecutive patients, 18 male with a median age of 68 years (range 29–77) were referred for PET/CT assessment of recurrent CRC. Indications for imaging were assessment of liver metastases ($n = 17$), rising CEA with normal routine imaging ($n = 7$), staging of recurrent disease ($n = 5$) and routine follow up in 2 patients with previously resected colorectal cancer. Median follow-up was 9.6 months (range 8–12) and 7 patients had histological follow-up. The remaining 24 patients were followed up with routine clinical and radiological assessment, with 7 of these patients having additional PET/CT.

PET/CT Protocol

One hour prior to the examination, 370MBq of ^{18}F -FDG was injected intravenously. Using a dedicated combined GE Discovery LS PET/CT unit {GE Advance PET scanner and the GE Light-speed CT (Michigan, USA)}, whole-body examinations were performed with the patient supine with arms held above the head (in those patients that could tolerate it). CT was performed using the four 3.75 mm detectors, a pitch of 1.5, and a 5mm collimation. The CT exposure factors for all examinations were 140 kVp and 80mA in 0.8secs. Maintaining patient position, a whole body PET emission scan was performed and covered an area identical to that by CT (covered by 5–6 bed positions). All acquisitions were carried out in 2D mode consisting of emission scans of 5 minutes per bed position. PET images were reconstructed using CT for attenuation correction by employing CT maps.

Fig. 1 The PET/CT scanner as seen by the patients (a) is shown. The view if the inside of the machine is also shown (b) with a full ring PET system (red arrows), with an X-ray CT gantry in front, showing the X-ray tube (white arrow head) and the bank of detectors (white arrows)

Transaxial emission images of $4.3 \times 4.3 \times 4.25 \text{ mm}^3$ (in plane matrix size 128x128) were reconstructed using ordered subsets expectation maximisation (OSEM) with two iterations and 28 subsets. The axial field of view was 148.75mm, resulting in 35 slices per bed position.

Image analysis

All images were interpreted by two experienced Nuclear Medicine physicians (A and B) without the clinical information. The PET images alone were initially reported and after a minimum six week period the PET/CT images were reported. For each patient, the observers identified the number of lesions seen and their anatomical localisation on a graded scale ranging from 0–2 (0 = unknown anatomical localisation, 1 = probable anatomical localisation and 2 = definite anatomical localisation). Certainty of diagnosis was also compared on a scale graded between 0–4 (0 = definitely benign, 1 = probably benign, 2 = equivocal, 3 = probably malignant, 4 = definitely malignant). Direct comparison of the results of the reported PET and PET/CT data was carried out on a lesion by lesion basis.

Discordant results between the PET/CT and the PET for an individual patient (not for each lesion) were all confirmed by histology when appropriate, or by routine clinical and radiological follow-up, including repeat PETCT if indicated. All imaging and management decisions were reviewed at multidisciplinary team meetings at a tertiary referral centre for recurrent CRC and decisions made were in consensus.

Results

Lesion reporting

Table 1 shows the total number of lesions identified by each observer using both PET/CT and PET alone. Definite anatomical localisation increased from 96 to 99% in Observer A and from 78% to 95% in Observer B. The percentage of lesions, which were reported as being certainly benign or malignant also increased from 86% to 99% for Observer A and from 72% to 94% for Observer B. PET/CT reduced the total number of lesions reported as malignant by correctly identifying normal focal uptake in loops of small

and large bowel. PET/CT also increased the certainty of diagnosis.

Inter-observer variability improved both anatomical localisation and certainty of diagnosis when combined PET/CT images were reported compared with PET images alone (Table 2).

Impact on surgical management

In 6 out of 31 cases (19%) there was an impact on surgical management. Two patients were downstaged using PET/CT. In one patient a presumed liver lesion was found to be physiological uptake in an unusually high hepatic flexure and in the second a presumed pelvic recurrence proved to be physiological uptake in a plunging loop of small bowel stuck into the pelvis post anterior resection. Two patients were upstaged to being inoperable by the identification of occult metastases. Two patients had improved anatomical localisation by PET/CT leading to an altered surgical incision with decreased morbidity. These six cases illustrate the diverse way that PET/CT affects clinical management when compared with PET alone (Figs. 2–5).

Discussion

This study demonstrates PET/CT over PET alone improves the accuracy of both staging and restaging in CRC thus positively impacted on the surgical management of recurrent colorectal cancer.

Improvement by both reporters in reducing the number of equivocal reports and increasing the number of definite reports is shown. This is vital with the modern multidisciplinary approach in the management of CRC and the increasing options for recurrent disease.

Patient management was changed in three different ways. Inappropriate liver resections were avoided in two patients due to the identification of further intra-abdominal disease with a further two patients avoiding inappropriate treatments due to down staging. The operative approach was altered in a further two patients.

Integrated PET/CT has already shown increased diagnostic accuracy over PET alone for the staging of non-small cell lung cancer [21, 22] There is similar evidence for other malignancies such as in the head and neck but at the

Table 1 Total number of lesions

	A		B	
	PET	PET/CT	PET	PET/CT
Total lesions identified	77	74	84	81
Definite anatomical localisation	96%	99%	78%	95%
Certainty of diagnosis	86%	99%	72%	94%

Table 2 PET/CT images compared with PET images

	¹⁸ F-FDG PET only		¹⁸ F-FDG PET/CT	
	Kappa coefficient	95% CI	Kappa coefficient	95% CI
Anatomical Localization	0.22 (Fair)	–0.08–0.51	0.66 (Good)	0.36–1.28
Certainty of diagnosis	0.62 (Good)	0.57–0.87	0.88 (V. good)	0.77–1.00

Fig. 2 The PET only images demonstrate a large FDG avid liver metastasis in the right lobe of the liver and two further lesions in the abdomen thought to be physiological uptake in the right ureter. The CT component suggests a 1cm lymph node adjacent to the right iliac vessels. The co-registered images allow identification of pathological FDG uptake in a right iliac lymph node. A non-curative liver resection is avoided.

Fig. 3 PET/CT accurately identifies a metachronous CRC in a patient with liver recurrence. On PET images alone it is unclear whether this is a local anastomotic recurrence, a nodal mass or other pathology. PET/CT co-registration allows for diagnostic accuracy. The patient underwent a successful resection.

present time the impact on other solid tumours including those of the pancreas [23], breast [24] and gynaecological tract [25, 26] is somewhat limited.

Whilst originally considered almost a side issue in the initial development of PET/CT technology, CT attenuation (density) correction has led to faster scanning times. Attenuation correction produces higher quality images by compensating for variations in density in the body. CT attenuation has eliminated the need for lengthy attenuation correction using radionuclide sources, which could take from 30 minutes to 1 hour to perform, compared with the rapid CT, which takes 30 seconds. This has increased the number of patients scanned in a working day from 6 to over 10, transforming a problem solving tool into a routine efficient clinical investigation [27].

PET/CT units are increasingly showing their utility by routinely producing high quality combined anatomical and metabolic information in a form which is quicker than dedicated PET scanning and user friendly for both the imager and the clinician alike. The latest technology with combined PET/CT scanners is becoming integrated into the management algorithm for CRC. In our institution this method has been enthusiastically accepted by both surgeons and oncologists and is likely to become the imaging modality of choice in a wide range of clinical problems, therapy monitoring and treatment planning, especially radiotherapy.

Both the PET/CT and the PET only images were reported by the same observers, therefore reducing blinding, however by having a minimal interval of two weeks between the reports this effect was minimised. The relatively

Fig. 4 PET only images reveal an area of increased uptake between liver and right kidney. It is difficult to tell whether this is pathological or physiological uptake at the splenic flexure or in the small bowel. CT suggests a small mass adjacent to Gerota's fascia and the co-registered images correctly identify an isolated recurrent tumour mass accounting for a rising CEA. This was resected through a local incision with CEA levels returning to normal.

Fig. 5 PET/CT accurately identifies localised recurrence in the absence of more disseminated disease. This lead to a change in incision from midline laparotomy to Lanz in a high risk patient with significant cardiac and respiratory co-morbidity.

small numbers in this study may be partially responsible for the inter-observer differences that are seen. This was particularly so for the PET only images. Importantly the inter-observer variability was greatly reduced for the PET/CT images due to the additional anatomical framework provided by integrated PET/CT systems.

This preliminary data demonstrates the potential advantages of integrated PET/CT over PET alone in reporting the images of patients with CRC. We have shown that the integration of PET and CT into a single modality allows information to become available which can significantly impact on the management of patients with CRC. Given that it is now accepted that multi disciplinary teams have fundamentally improved the management of CRC, PET/CT imaging further enhances this approach by visualising both the function and morphology of colorectal cancer.

Conflict of interest The authors do not have any disclosable interest

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